

# Nanoparticles can improve the positive rate of metastatic lymph node in thyroid cancer surgery

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## Research

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# Abstract

## Objective.

To investigate the application of carbon nanoparticles in lymph node dissection and parathyroid gland protection during thyroid cancer surgery.

## Subjects and Methods.

Retrospective analysis was performed on 282 cases of thyroid cancer surgery in our hospital from 2018 to 2019. All patients underwent total thyroidectomy and cervical central lymph node dissection. Nanocarbon was not used in the control group, but was used in the experimental group. The general situation of the patients, the number of postoperative lymph nodes and the number of metastasis were collected, and the differences between serum parathyroid hormone and blood calcium were compared before and on the 3rd and 30th day after surgery.

## Results.

There was no difference in age, sex and TNM stage between the two groups ( $P > 0.05$ ). The number of metastatic lymph nodes in the experimental group ( $9.80 \pm 4.80$ ) was different from that in the control group ( $6.95 \pm 3.86$ ) ( $P < 0.05$ ), and the number of metastatic lymph nodes in the experimental group was different from that in the control group ( $\chi^2 = 14.968$ ,  $P < 0.05$ ). There was no difference in blood calcium and PTH between the two groups before and at 3 and 30 days after surgery ( $P > 0.05$ ).

## Conclusion.

The application of carbon nanoparticles in thyroid cancer surgery can significantly increase the number of lymph nodes seized and the positive rate of metastatic lymph node removal, but the protection of parathyroid gland is not obvious.

## Background

Thyroid cancer is the most common endocrine malignant tumor, and the most common pathological type is papillary thyroid cancer (PTC), accounting for more than 90% of the total thyroid cancer<sup>1-2</sup>. Surgical treatment is the main treatment of this disease<sup>3</sup>, because of its high rate of lymph node metastasis<sup>4</sup>; therefore, the routine cervical lymph node dissection in China increases the injury rate of parathyroid gland and the risk of postoperative hypocalcaemia with the expansion of surgical scope<sup>5</sup>. Studies have shown that carbon nanoparticles can darken lymph nodes and negatively develop parathyroid glands<sup>6</sup>; it is widely used in thyroid surgery, but whether carbon nanoparticles have a protective effect on

parathyroid glands is controversial<sup>10,17</sup>.The purpose of this study was to investigate the value of carbon nanoparticles in thyroid cancer surgery and cervical central lymph node dissection.

## **Subjects And Methods**

### **1.1 Case data**

This study is a retrospective analysis of relevant case data from the first affiliated hospital of Jinzhou Medical University, and does not involve ethical issues.The clinical data of 282 patients who underwent surgical treatment for thyroid cancer in our department from January 2018 to June 2019 were retrospectively analyzed. Inclusion criteria were :(1) all patients underwent total thyroidectomy and underwent unilateral or bilateral cervical central lymph node dissection (2) all patients had no distant metastasis. (3) thyroid papillary carcinoma was confirmed pathologically (4) thyroid surgery was performed for the first time (5) preoperative imaging showed no lymph node metastasis in the cervical region (6)preoperative PTH and blood calcium measurements were within the normal range. Exclusion criteria were :(1) diseases associated with abnormal PTH and blood calcium; (2) history of neck surgery and radiotherapy; (3) preoperative parathyroid dysfunction; (4) metastases to other malignant tumors involving the thyroid; (5) pregnant or lactating women. Patients were randomly divided into the experimental group and the control group. The experimental group was given intraoperative carbon nanoparticles, while the control group was not. Age, sex, tumor size, tumor infiltration in capsule and surrounding muscles, TNM staging (the 8th edition of the American joint commission on cancer AJCC thyroid cancer TNM staging, 2017) and other basic information were collected. The number of lymph nodes removed and the number of metastatic lymph nodes in the two groups were counted. PTH and serum calcium values were measured preoperatively and at 3 and 30 days postoperatively. The nano carbon suspensions used in the operation were all products of Chongqing Lummy Pharmaceutical Co.Ltd.

### **1.2 surgical methods**

All patients underwent total thyroidectomy and cervical central lymph node dissection. The thyroid gland was routinely exposed. In the experimental group, 0.1ml of carbon nanoparticles was injected into the affected side at 1-2 points through a 1ml syringe. After that, the injection point was pressed with gauze to prevent nano-carbon leakage. After 10min, the lymph nodes were blackened and then the adenoidectomy was performed. During the operation, the thyroid papillary carcinoma was confirmed by rapid freezing pathology. Intraoperative attention was paid to fine dissection of thyroid capsule. The number of lymph nodes removed and the number of metastatic lymph nodes were compared between the two groups.

### **1.3 statistical analysis**

The collected clinical data were statistically analyzed by SPSS 22 software. The counting data were expressed as a percentage (%), and 2 test were performed. The measurement data is expressed by t test.  $P < 0.05$  was considered statistically significant.

# Result

## 2.1 comparison of basic conditions between the two groups

There was no significant difference in age, gender, tumor size and TNM stage between the experimental group (162 cases) and the control group (120 cases) ( $P > .05$ ), as shown in table 1.

## 2.2 Lymph node detection

The total number of lymph nodes detected in the experimental group was 1587, compared with 810 in the control group, the difference was statistically significant ( $P < 0.05$ ). The detection of metastatic lymph nodes in the experimental group was significantly different from that in the control group ( $P < 0.05$ ). See table 2 for details.

## 2.3 Postoperative changes in serum calcium and PTH

There was no significant difference in serum calcium and PTH levels between the two groups before and after 3 and 30 days, as shown in table 3.

# Discuss

Papillary carcinoma of the thyroid (PTC) is the most common thyroid malignancy, with lymph node metastasis rates reported to be as high as 50-70% in patients with PTC<sup>7</sup>, However, incomplete intraoperative lymph node dissection is an important factor causing postoperative recurrence in patients, and expanding the scope of dissection will increase the risk of damage to the parathyroid gland. The position of the superior parathyroid gland is relatively fixed, while the position of the inferior parathyroid gland varies greatly<sup>8</sup>, Multiple lymph node metastases often require extensive dissection, which may damage the parathyroid gland or even cut it by mistake, seriously affect the prognosis and quality of life of patients, and even threaten the life of patients. Therefore, how to protect the parathyroid gland while removing lymph nodes is the key.

Carbon nanoparticles with an average diameter of 150nm can enter lymphatic vessels (with an average diameter of 500nm) rather than capillaries (with an average diameter of 30-50nm), allowing the development of lymph nodes. Since the lymphatic vessels of thyroid gland and parathyroid gland do not communicate with each other, most scholars believe that negative development of parathyroid gland has a protective effect on it, and it has been widely used in thyroid cancer surgery in recent years<sup>9</sup>. The results of this study showed that there was a significant statistical difference between the experimental group and the control group in the total number of lymph nodes cleared and the positive rate of metastatic lymph nodes. Consistent with the views of Luo Wenzheng and other researchers<sup>10-</sup>

<sup>12</sup>11111111111156456466—[[i]222115415, Considering carbon nanoparticles can help surgeons better identify lymph nodes in the central region, especially the microscopic nodes that are difficult to be distinguished by the naked eye, reduce lymph node residues, and make it easier and more accurate for

pathologists to extract lymph nodes<sup>13</sup>. Together, the two can increase the number of lymph nodes detected, and the corresponding seizure rate of metastatic lymph nodes is also improved, which is conducive to more accurate postoperative judgment of staging and prognosis, as well as elimination of potential sources of lymph node recurrence<sup>14-15</sup>. However, there was no statistical difference in the changes of blood calcium and PTH between the experimental group and the control group at 3 and 30 days after surgery ( $P > 0.05$ ), which was consistent with the views of Liu et al<sup>16-17</sup>] that is, the parathyroid protection is not significant. We think it may be caused by the following reasons: The recognition of parathyroid gland is closely related to the surgical experience of surgeons. Experienced physicians can completely identify the parathyroid gland by the color, texture and appearance of the parathyroid gland with the naked eye, without other development techniques to protect the parathyroid gland. In some cases, intraoperative leakage may occur due to improper handling of nanocarbons. In this case, the wound may be contaminated, making it impossible for the accessory glands to identify the nanocarbons and causing accidental injury. For small glands the dose of carbon nanoparticles should be reduced.

In conclusion, although nanocarbon does not significantly protect the parathyroid gland, it can significantly improve the number of seized lymph nodes and the positive rate of metastatic lymph node removal, facilitate accurate postoperative judgment of the stage and prognosis of patients, and reduce the recurrence rate. Therefore, nanocarbon is worth promoting for young doctors and doctors in primary hospitals. The sample size included in this study is relatively small, and there is a lack of research on longer follow-up and survival analysis of patients, so more in-depth research is needed to explore its use value.

## Conclusion

We found that the application of carbon nanoparticles in thyroid cancer surgery can significantly increase the number of detected lymph nodes and the positive rate of metastatic lymph node clearance, but the protection of parathyroid gland is not obvious. A larger sample study may be needed.

## List Of Abbreviations

TNM: Tumor Node Metastasis

PTH: parathyroid hormone

PTC: papillary thyroid cancer

AJCC: American Joint Committee on cancer

## Declarations

**Ethics approval and consent to participate**

Comrade XinDi Su Contribution to Your Edition: Nanoparticles can improve the positive rate of metastatic lymph node in thyroid cancer surgery. Confirmed by the Medical Ethics Committee of the First Affiliated Hospital of Jinzhou Medical University, the purpose of the paper, the research process, the source of the material, and the ethical matters of medical research were reviewed and passed, and the patients were informed by ethical principles. NO.KYLL202005.

After the initial audit, medical research ethical matters in line with the "Helsinki Declaration" and the Ministry of Health "involving human biomedical research ethical review method (Trial)" requirements. The medical ethics committee of our hospital will follow up the supervision of the relevant items of medical ethics research after the approval of the project.

Sign: The First Affiliated Hospital of Jinzhou Medical University Medical Ethics Committee.

#### **Consent for publication**

Not applicable

#### **Availability of data and materials**

Not applicable

#### **Competing interests**

The authors declare that they have no competing interests.

#### **Funding**

Not applicable

#### **Authors' contributions**

XinDi Su, draft, manuscript writing, study design, data collection, approval, agreement; Fang Chai, study design, draft, revise, approval, agreement; BenRui Lin, study design, revision, approval, agreement; Lu Qu, study design, revision, approval, agreement; KeYi Liu, data collection, editing of the article, approval, agreement; JianPingHuo, study, design, approval, agreement; ZhanSheng Zhu, study design, revision; Rashid, editing of the article.

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## Tables

Table 1 basic situation analysis table of the two groups of patients

Basic situation	The experimental group	The control group	$\chi^2/t$	<i>P</i>
Age	47.24±11.72	51.38±12.03	1.672	0.098
Sex			0.091	0.762
Male	15□9.3%□	9□7.5%□		
Female	147□90.7%□	111□92.5%□		
Tumor size	1.39±0.85	1.64±0.85	1.422	0.158
TNM			3.027	0.082
□	135□83.3%□	114□95%□		
□	27□16.7%□	6□5%□		
Capsule infiltration			0.625	0.429
Yes	57□35.2%□	33□27.5%□		
No	105□64.8%□	87□72.5%□		
Muscle infiltration			1.008	0.315
Yes	33□20.4%□	15□12.5%□		
No	129□79.6%□	105□87.5%□		
Central lymph node dissection			3.197	0.074
Unilateral				
bilateral	63□38.9%□	69□57.5%□		
	99□61.1%□	51□42.5%□		

Table 2 statistical table of lymph node detection in the two groups

Group	Number	Total lymph node clearance	Number of metastatic lymph nodes [%]
The experimental group	162	9.80±4.80	276±17.39±
The control group	120	6.95±3.86	237±29.26±
$\chi^2/t$		3.084	14.968
$P$		0.003	0.001

Table 3 statistical table of changes of serum calcium and blood PTH before surgery, 3 days after surgery and 30 days after surgery

Group	Before the operation	3 days after surgery	30 days after surgery
The experimental group PTH	60.47±19.24	29.74±14.15	57.74±24.29
The control group PTH	61.46±20.70	36.53±19.68	50.45±18.34
t	0.239	1.855	1.591
$P$	0.812	0.068	0.115
Experimental group serum calcium	2.34±0.12	2.20±0.16	2.33±0.11
Control group serum calcium	2.31±0.14	2.21±0.13	2.29±0.14
t	1.136	0.326	1.597
$P$	0.259	0.745	0.114